

REPLY AND AMENDMENT

Serial No.: 09/849,781

Filing Date: May 4, 2001

Title: Protein Chips for High Throughput Screening
of Protein Activity

Atty. Dkt. No. 0618.013.0002

REMARKS/ARGUMENTS

I. AMENDMENTS TO THE SPECIFICATION AND CLAIMS

The specification has been amended to remove embedded hyperlinks and to correct a typographical error. Thus, no new material has been added by way of the amendments to the specification. The objection to the specification is now moot in light of the amendments to the specification.

Claims 187 and 189-191 have been canceled, without prejudice or disclaimer, solely to expedite prosecution, and Applicants reserve the right to pursue the canceled claims in one or more divisional, continuation or continuation-in-part applications. No pending claims have been amended.

II. THE REJECTIONS UNDER 35 U.S.C. §112, FIRST PARAGRAPH ARE TRAVERSED OR MOOT

A. THE REJECTION OF CLAIMS 1-11, 141, 164, 166, 169, 170, 173, 177, 178 AND 181-192 UNDER 35 U.S.C. §112, FIRST PARAGRAPH (WRITTEN DESCRIPTION) IS TRAVERSED

1. The Rejection

The Office Action dated March 18, 2005, alleged that claims 1-11, 141, 164, 166, 169, 170, 173, 177, 178 and 181-192 are not patentable because the specification fails to comply with the written description requirement under 35 U.S.C. §112, first paragraph. Applicants respectfully disagree with the Office Action's assertions that the referenced claims are not supported by the specification and traverse this rejection.

Specifically, the Office Action states that the "specification disclosure does not sufficiently teach the claimed array wherein the kinases ... derive from *any* mammal or *any* *Drosophila*." *Prosecution History of U.S. Serial No. 09/849,781, Office Action dated March 18,*

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2005, page 7 (emphasis in original). In addition, the Office Action states that, “[w]ith the exception of a yeast protein kinase array, wherein the array comprises 122 different yeast kinases, disclosed by the specification, the skilled artisan cannot envision the claimed array wherein the kinases ... derive from *any* mammal or *any* Drosophila.” *Office Action*, page 7 (emphasis in original). In support of her assertions that the specification fails to provide adequate written description for the claimed subject matter, the Office Action cites *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555 (Fed. Cir. 1991) for the proposition that specification must “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” *Vas-Cath* at 1563 (quoting *In re Gosteli*, 872 F.2d 1008, 1012 (Fed. Cir. 1989) (alterations in original).

The Office Action also cites other well-known cases in which the Board or the Federal Circuit has addressed the written description requirement in the context of biotechnology. The Office Action cites *Fiers v. Revel*, 984 F.2d 1164 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 927 F.2d 1200 (Fed. Cir. 1991) after asserting that [a]dequate written description requires more than a mere statement that it [DNA] is part of the invention and reference to a potential method for making and using it.” *Office Action*, page 7. The Office Action also cited *Fiddes v. Baird*, 1993 Pat. App. LEXIS 21, 30 U.S.P.Q. 2d 1481(B.P.A.I. 1993), where, according to the Office Action, the Board held that claims that were directed to mammalian FGFs (fibroblast growth factors) were unpatentable “due to lack of written description for the broad class [of mammalian FGFs]” *Office Action*, page 8. Finally, the Office Action quotes from *Regents of the University of California v. Eli Lilly and Co.*, 119 F.3d 1559 (Fed. Cir. 1997), in which the Federal Circuit discussed what was, at the time, the status of the written description requirement as it related to biotechnology.

Applicants respectfully disagree with the Office Action’s assertion that the specification fails to provide written description for the pending claims, in view of the cited case law. Applicants also assert that the cited cases are inapplicable to the pending application. First, in each of the cases the Office Action cites, the claims at issue were *directed towards* novel DNA or

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protein molecules themselves, rather than methods or compositions involving proteins. Second, in each of the cited cases, the claims were directed to novel DNA or protein molecules, where the identity of the molecule was *unknown* prior to the filing date of the patents at issue.

For example, in *Fiers*, most of the DNA that was claimed was “DNA which consists essentially of a DNA which codes for a human fibroblast interferon-beta polypeptide,” where the nucleotide sequence was entirely unknown. *Fiers* at 1166. In *Amgen*, the claims at issue were directed to erythropoietine (EPO), and the structure of the EPO DNA sequence was unrecognized at the time of filing the application. In *Fiddes*, the count at issue in the interference was directed towards a DNA encoding mammalian basic fibroblast growth factor, although the invention “provide[d] the first known pure mammalian FGF” and the patent taught “no amino acid or DNA sequence for any mammalian FGF other than bovine pituitary FGF.” *Fiddes*, 1993 Pat. App. LEXIS at 5, 8, respectively. In *Lilly*, the claims were directed to human insulin cDNA, although human insulin DNA had never been characterized.

The cases upon which the Office Action relies are inapplicable to the pending application, because, unlike the facts behind the cited cases, the pending claims are not directed towards novel DNA or proteins. And, more importantly, none of the cases upon which the Office Action relies imposes the duty of reanalysis of molecules whose structures are already known and part of the state of the art. The Federal Circuit has addressed the written description requirement in the context of biotechnological patents, where the claims simply utilize biological materials that are not new or unknown. In *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313 (Fed. Cir. 2003), the claims at issue were directed to types of cells that could be used to produce human EPO, and the court stated that “[the] Eli Lilly [decision] ... [is] inapposite to this case because the claim terms at issue here are not new or unknown biological materials that ordinarily skilled artisans would easily miscomprehend.” *Amgen v. Hoechst* at 1332. The court then stated that the challengers to the Amgen-owned patent at issue “can only challenge the adequacy of the disclosure of the ... host cell – not the human DNA itself.” *Id.* Similar to the facts in *Amgen v.*

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Hoechst, the claims here are not directed towards DNA or proteins themselves, and the claim terms here do not utilize “new or unknown biological materials that the ordinarily skilled artisan would easily miscomprehend.” Rather, the claims of the pending application are directed towards arrays comprising kinases or functional domains thereof. The sufficiency of the disclosure in supporting the currently pending claims, therefore, must be analyzed in light of a “positionally addressable array,” rather than kinases, which were well known as of the filing date of the present application. Applicants assert that, when viewed in the proper context, the specification fully describes the claimed subject matter as it relates to an array comprising kinases or functional domains thereof.

In addition, in each of the cases upon which the Office Action relies, most, if not all, of the *claimed* DNA or protein had not been previously characterized. In the pending application at hand, Applicants assert that the identity of the eukaryotic kinase superfamily was known prior to the filing date of the present application. For example, in *Hanks, S.K. and Hunter, T., FASEB J.*, 9:576-596 (1995), the authors state that, as of 1995, “there are now hundreds of different members [of the kinase superfamily] whose sequences are known.” *Hanks and Hunter*, page 576. Furthermore, kinases were already readily recognized in 1995 “by virtue of their kinase domains...that...contain 12 conserved subdomains that fold into 3-dimensional structures of several protein-serine kinases.” *Hanks and Hunter*, page 576 (abstract). Indeed, Figure 1 of *Hanks and Hunter* depicts the conserved features of the kinase domain primary structure, even though the sequences are “drawn ... from the widest possible sampling of the superfamily, and thus provide a good representation of the known primary structures.” *Hanks and Hunter*, page 577-587. Furthermore, methods that could be used to confirm kinase activity were well known as of the filing date of the present application. Thus protein kinases, and functional domains thereof, were well-known in the art at the time of filing the application.

The written description requirement must be viewed in light of the state of the art at the time of filing. Applicants assert that, when viewed in light of the state of the art at the time of

filing the present application, the specification fully supports the claimed array of claims 1-11, 141, 164, 166, 169, 170, 173, 177, 178 and 181-192, because kinases from not only yeast, but also from any mammal or any *Drosophila* could be readily recognized, based on the well-known conserved structural motifs of the hundreds of known kinases as of the filing date of the pending application. And as the Federal Circuit has recently stated that “[t]he descriptive text needed to meet these [written description] requirements varies with the nature and scope of the invention as issue, and with the scientific and technologic knowledge already in existence.” *Capon et al. v. Eshhar et al. v. Dudas* 2005 U.S. App. LEXIS 16865, 20 (Fed. Cir. Aug. 12, 2005)

2. The Recent Clarification of Written Description from the Federal Circuit

Even more relevant to the presently claimed invention, the Federal Circuit, in overturning a decision by the Board of Patent Appeals and Interferences (“the Board”), recently clarified the written description requirement in the context of claims that utilize known biological materials in *Capon et al. v. Eshhar et al. v. Dudas*, 2005 U.S. App. LEXIS 16865 (Fed. Cir. Aug. 12, 2005), a copy of which is enclosed for the Examiner’s convenience. In fact, *Capon* was decided and published *after* the mailing date of the March 18th Office Action. Specifically, *Capon* clarifies the written description requirement as delineated by *Fiers, Amgen v. Chugai* and *Eli Lilly*, which are the exact cases the Office Action relies upon in its written description rejections in the outstanding office action of the present application.

In *Capon*, the claims involved in the interference were directed to a chimeric gene, which “combines segments of DNA in a way that does not occur in nature.” *Capon* at 4. The DNA components of the chimeric genes were “*known* antigen-binding-domain producing DNA and *known* lymphocyte-receptor-protein producing DNA.” *Capon* at 4-5 (emphasis added). The Board, however, held that “neither party’s specification provides the requisite description of the full scope of the chimeric DNA or encoded proteins....” *Capon* at 13. In support of their

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decision, the Board cited *Eli Lilly, Fiers, Amgen v. Chugai* and *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 296 F.3d 1316 (Fed. Cir. 2002) as controlling precedent. But in challenging the Board's decisions, the Appellants asserted that the "requirement that the specification must reproduce the 'structure, formula, chemical name, or physical properties' of [the] DNA combinations had been *overtaken by the state of the science*." *Capon* at 16 (emphasis added).

In discussing the current state of the written description requirement under 35 U.S.C. §112, first paragraph, the Federal Circuit stated that "[s]ince the law is applied to each invention *in view of the state of relevant knowledge*, its application [the written description requirement] will vary with differences in the state of knowledge in the field" *Capon* at 21 (emphasis added). In reviewing and overturning the Board's decision, the Federal Circuit held that "[t]he Board erred in refusing to consider the state of scientific knowledge...." *Capon* at 21. Furthermore, the Federal Circuit stated that the Board's reliance on *Eli Lilly, Fiers, Amgen v. Chugai* and *Enzo* for the case at bar was incorrect and explained that "[n]one of the cases to which the Board attributes the requirement of total DNA re-analysis, *i.e.*, *Regents v. Lilly, Fiers v. Revel, Amgen [v. Chugai]*, or *Enzo Biochem*, require a re-description of what was already known." *Capon* at 21. The Federal Circuit elaborated that "[t]he Board's rule that the nucleotide sequences of the chimeric genes must be fully presented, although the nucleotide sequences of the component DNA are known, is an inappropriate generalization." *Capon* at 23. It is particularly noteworthy that the Federal Circuit made this assertion that nucleotide sequences need not be fully presented to satisfy the written description requirement, because the sequences of a sufficient number of sequences of the DNA chimera components were available in the published literature and methods were known and provided for linking the components of the chimera. *Capon* at 15.

Thus, the Federal Circuit not only clarified the requirements for written description in the context of known biological materials, but also reiterated that a proper written description analysis must take into account "the state of scientific knowledge." Similar to the facts

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surrounding Capon, the structural motifs of kinases that are to be utilized in the claimed array were delineated well before the filing of the present application and claims. Indeed, kinases and their functional domains were well known in the art as of 1995. *See Hanks and Hunter, supra*. Furthermore, one of skill in the art could even review the DNA sequence of a coding sequence or amino acid sequence of a novel protein and easily determine that the coding sequence coded for a kinase or that the novel protein was, in fact, a kinase, based on these well-known structural motifs and publicly available nucleotide and protein sequence information. These well-known motifs could be used to identify additional mammalian kinases and *Drosophila* kinases from at least those motifs specifically identified on or after the publication *Hanks and Hunter* in 1995, five years before the priority date of the present application. For example, in Morrison, D.K., *et al.*, *J. Cell Bio.*, 150(2):F57-62 (July, 2000), the authors were able to identify approximately 251 *Drosophila* kinases, based on analyzing the *Drosophila* genome using automated gene predictor methods, and comparing sequences to the kinase structural motif. The *Drosophila* genome was published *prior* to the filing date of the application and was thus part of the state of scientific knowledge at the time of filing the present application. *See Adams, M.D., et al, Science*, 287:2185-2195 (2000) (copy enclosed).

Also illustrative of the state of art at the time of or before the filing of the present application, Plowman *et al.*, *Proc. Natl. Acad. Soc.*, 96:13603-13610 (November 1999) (copy enclosed), discloses specific bioinformatics tools that were used to identify kinases from genomic information of *C. elegans* using the well-known conserved kinase structural motifs to identify 411 worm kinases. The authors also used these same bioinformatics tools to assess publicly available expressed sequence tag data to identify 592 human kinases. (*Plowman et al.*, 13604, *left column and Table 1*). Accordingly, using bioinformatics tools, such as those disclosed in Plowman *et al.* and Morrison *et al.* in conjunction with the publicly available sequence information, a skilled artisan would recognize that, as of the filing date of the present application, the sequences of virtually any kinase from any mammal or any *Drosophila* were either readily

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available or easily identifiable. Applicants assert, therefore, that the state of the art as of the filing date of the present application was such that one of skill in the art would be able to recognize a DNA sequence encoding a kinase or a kinase amino acid sequence from any mammal or any *Drosophila*, without further guidance from the present specification. Accordingly, Applicants believe that the present specification adequately and sufficiently describes the presently claimed subject matter, in view of the state of the art at the time the application was filed. Reconsideration and withdrawal of this rejection are earnestly solicited.

B. THE REJECTION OF CLAIMS 1-11, 141, 164, 166, 169, 170, 173, 177, 178 AND 181-192 UNDER 35 U.S.C. §112, FIRST PARAGRAPH (WRITTEN DESCRIPTION) IS TRAVERSED

The March 18th Office Action alleged that claims 1-11, 141, 164, 166, 169, 170, 173, 177, 178 and 181-192 are not patentable because the specification fails to comply with the written description requirement under 35 U.S.C. §112, first paragraph. Applicants respectfully disagree with the Office Action's assertions that the referenced claims are not supported by the specification and traverse this rejection. The Office Action alleges that the specification "clearly does not provide an adequate representation regarding the claimed array wherein the plurality of different substances is [a] kinase analog (refers to the limitation of 'molecules comprising functional domains thereof')" *Office Action*, page 8.

Similar to the comments presented above, Applicants assert that the specification, when viewed in light of the state of scientific knowledge at the time of filing, adequately supports the claimed invention. Specifically, as discussed above, the structural motifs of kinases were well known prior to filing the present application. In fact, functional domains of kinases are the motifs that define the group and give them their functional activity. See *Hanks and Hunter, supra*. Furthermore, the functional kinase domains were very well understood with respect to their structure as of the filing date of the present application. See *Hanks and Hunter, supra*.

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As in the arguments presented above, Applicants assert that the Office Action's reliance on *Fiers, Amgen v. Chugai, Fiddes and Eli Lilly* is misplaced, in view of recent Federal Circuit case law that clarifies the written description requirement, *See Capon* and *Amgen v. Hoechst*. Accordingly, in light of the state of scientific knowledge at the time of filing the present application, and in view of Federal Circuit precedent that states that "re-description of what [is] already known" is not required for adequate written description, Applicants assert that the present specification fully supports the claimed invention as it relates to "functional domains" of kinases, from any mammal or any *Drosophila*. Reconsideration and withdrawal of this rejection are earnestly solicited.

C. THE REJECTION OF CLAIMS 1, 187 AND 189-191 UNDER 35 U.S.C. §112, FIRST PARAGRAPH (WRITTEN DESCRIPTION) IS MOOT

The March 18th Office Action rejected claims 1, 187 and 189-191 under 35 U.S.C. §112, first paragraph, because the specification allegedly fails to support the claimed invention. Without agreeing with the Office Action's assertions, Applicants have canceled claims 187 and 189-191, without prejudice or disclaimer, thus rendering moot the Office Action's rejection as it relates to claims 187 and 189-191.

Applicants, however, respectfully disagree with the Office Action's characterization of claim 1. Claim 1 does not claim an array "wherein the plurality of different substances comprises all of the kinases of an organism" *Office Action*, page 13. Solely to expedite prosecution, and to minimize the number of rejections at issue, Applicants have canceled claims 187 and 189-191, which claimed an array comprising all the kinases of an organism. Claim 1, however, does not contain such a limitation. Reconsideration and withdrawal of this rejection, as it relates to claim 1 are earnestly solicited.

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D. THE REJECTION OF CLAIMS 1, 187 AND 189-191 UNDER 35 U.S.C. §112, FIRST PARAGRAPH (ENABLEMENT) IS MOOT

The March 18th Office Action rejected claims 1, 187 and 189-191 under 35 U.S.C. §112, first paragraph, because the specification allegedly fails to enable the claimed invention. Without agreeing with the Office Action's assertions, Applicants have canceled claims 187 and 189-191, without prejudice or disclaimer, thus rendering moot the Office Action's rejection as it relates to claims 187 and 189-191.

Applicants, however, respectfully disagree with the Office Action's characterization of claim 1. Claim 1 does not claim an array that "comprises all of the protein kinases ... of a single organism" *Office Action*, page 19. Solely to expedite prosecution, and to minimize the number of rejections at issue, Applicants have canceled claims 187 and 189-191, which claimed an array comprising all the kinases of an organism.

Claim 1, however, does not contain the limitation that the array comprise all of the kinases of an organism. In the view of the state of the art at the time of filing, Applicants assert that the specification fully enables claim 1. See *Hanks and Hunter, supra*. Reconsideration and withdrawal of this rejection, as it relates to claim 1 are earnestly solicited.

E. THE REJECTION OF CLAIM 187 UNDER 35 U.S.C. §112, SECOND PARAGRAPH, IS NOW MOOT

The March 18th Office Action rejected claim 187 under 35 U.S.C. §112, second paragraph, for allegedly "being indefinite for failing to particularly point out and distinctly claim the subject which applicant regards as the invention." *Office Action*, page 19. Without agreeing with the Office Action's assertions, Applicants have canceled claim 187, without prejudice or disclaimer, thus rendering moot the Office Action's rejection. Reconsideration and withdrawal of this rejection are earnestly solicited.

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CONCLUSION

Applicants have amended the specification to overcome the outstanding rejections and to correct a typographical error, and have canceled claims 187 and 189-191, without prejudice or disclaimer, solely to expedite prosecution. Applicants have traversed the outstanding rejections of the claims under 35 U.S.C. §112, first paragraph and assert that the specification fully describes and enables the claimed invention.

Should the Examiner believe that further discussion of any remaining issues would advance the prosecution, he or she is invited to contact the undersigned at the telephone number listed below.

Respectfully submitted,

Date September 19, 2005 By Todd B. Buck

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